

Substitute for form 1449A/PTO


**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet

1

of

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Complete if Known

Application Number	10/669,099
Filing Date	September 22, 2003
First Named Inventor	Gorfine, Stephen R.
Art Unit	1654
Examiner Name	Tate, Christopher Robin
Attorney Docket Number	010692-004532US

U.S. PATENT DOCUMENTS+

Examiner Initials	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number Kind Code ² (if known)			
	1	US-814,408	03-06-1906	Steele	
	2	US-2,840,080	06-24-1958	Clark	
	3	US-3,419,571	12-31-1968	Di Carlo et al.	
	4	US-4,118,480	10-03-1978	Williams	
	5	US-4,226,849	10-07-1980	Schor	
	6	US-4,292,299	09-29-1981	Suzuki et al.	
	7	US-4,371,516	02-01-1983	Gregory et al.	
	8	US-4,514,384	04-30-1985	Gallina	
	9	US-4,608,249	08-26-1986	Otsuka et al.	
	10	US-4,654,209	03-31-1987	Leslie et al.	
	11	US-4,657,906	04-14-1987	Emmet et al.	
	12	US-4,683,242	07-28-1987	Poser	
	13	US-4,746,675	05-24-1988	Makino et al.	
	14	US-4,842,854	06-27-1989	Babalan et al.	
	15	US-5,047,230	09-10-1991	Nagy et al.	
	16	US-5,059,603	10-22-1991	Rubin	
	17	US-5,085,650	02-04-1992	Giglio	
	18	US-5,183,663	02-02-1993	Greiner	
	19	US-5,439,938	08-08-1995	Snyder et al.	
	20	US-5,504,117	04-02-1996	Gorfine	
	21	US-5,508,045	04-16-1996	Harrison et al.	
	22	US-5,595,753	01-27-1997	Hechtman	
	23	US-5,595,970	01-21-1997	Garfield et al.	
	24	US-5,693,676	12-07-1997	Gorfine	

FOREIGN PATENT DOCUMENTS

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		Number ⁴	Country Code ³ Kind Code ⁵ (if known)				
	25	DE 304,730		03-01-1989	Dunzendorfer et al.		<input type="checkbox"/>
	26	AU 74545/94		08-19-1994	Koren Laboratories Pty., Ltd.		<input type="checkbox"/>
	27	AU PM 0971		03-22-1995	Koren Laboratories Pty., Ltd.		<input type="checkbox"/>
	28	AU PM 4247		03-22-1995	Koren Laboratories Pty., Ltd.		<input type="checkbox"/>
	29	AU PM 6395		07-14-1994	Koren Laboratories Pty., Ltd.		<input type="checkbox"/>
	30	DE 4,038,203		06-04-1992	Bonacker et al.		<input type="checkbox"/>
	31	JP 62-67017		03-26-1987	Sawai et al.		<input type="checkbox"/>
	32	WO 98/36733		08-27-1998	Kamm, Michael Albert et al.		<input type="checkbox"/>

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C. R. Tate

Date Considered

12/12/05

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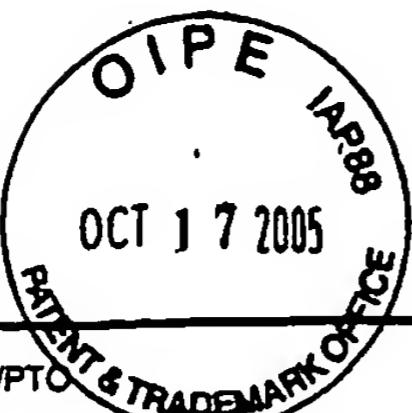
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<p>Substitute for form 1449A/PTO</p> <p>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</p> <p><i>(use as many sheets as necessary)</i></p>				Complete if Known	
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				Examiner Name	Tate, Christopher Robin
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BB	33	WO	95/06466	A1	03-09-1995	Koren Laboratories Pty., Ltd.
BB	34	ZA	77/01135		02-25-1977	Prinsloo, J.
BB	35	JP	04-091036		03-24-1996	Hashioka Tatsuya
BB	36	WO	87/03490		06-18-1987	Key Pharmaceuticals, Inc.
BB	37	WO	98/37886		09-03-1998	Antropoli

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NON PATENT LITERATURE DOCUMENTS				
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	38	Ahlner et al., "Organic Nitrate Esters: Clinical Use and Mechanisms of Actions." <i>Pharmacol. Reviews</i> 43(3):351-353 (1991).		T ²
	39	Budavari et al. (Eds.), "The Merck Index." pp. 198 and 821 (isopropyl nitrate); 11th Edition, Merck & Co., Rahway, N.J. (1989)		
	40	Bult et al., "Nitric oxide as an inhibitory non-adrenergic non-cholinergic neurotransmitter." <i>Nature</i> , 345:346-347, 1990.		
	41	Burleigh, D. and D'Mello, A., "Physiology and Pharmacology of the Internal Anal Sphincter." Chapter 2, pages 22-41, in <i>Coloproctology and The Pelvic Floor</i> , Henry and Swash (Eds.), Butterworth Publishers, Stoneham, Mass., USA and London, England, ISBN 0-407-00352-5 (1985)		
	42	Burleigh, D., "Ng-Nitro-L-Arginine Reduces Nonadrenergic Relaxations of Human Gut." <i>Gastroenterology</i> , 102: 679-683 (1992)		
	43	Chakder, et al. "Release of nitric oxide by activation of nonadrenergic noncholinergic neurons of internal anal sphincter." <u>NO Release By Nanc Neural Stimulation and VIP</u> , G7-12 (1992)		
	44	Enck et al., "Spontaneous variation of anal 'resting' pressure in healthy humans." <i>Am. J. Physiol.</i> , 261(5 Pt 1):G823-G826 (1991)		
	45	Farouk et al., "Sustained Internal Sphincter Hypertonia in Patients with Chronic Anal Fissure." <i>Dis. Col. Rect.</i> , 37:424-429 (1994)		
	46	Feehleisch et al., "Correlation between nitric oxide formation during degradation of organic nitrates and activation of guanylate cyclase." <i>Eur. J. Pharmacol.</i> , 139:19-30 (1987)		
	47	Fung et al., "Biochemical mechanism of organic nitrate action." <i>Am. J. Cardiol.</i> , 70:4B-10B (1992)		
	48	Gibbons et al., "Anal hypertonia in fissures; cause or effect?" <i>Br. J. Surg.</i> , 73:443-445 (June 1986).		
	49	Gillespie et al., "Influence of hemoglobin and erythrocytes on the effects of EDRF, a smooth muscle inhibitory factor, and nitric oxide on vascular and non-vascular smooth muscle." <i>Br. J. Pharmacol.</i> , 95:1151-1156, 1988.		
	50	Gorfine, SR., 1995, "Treatment of benign anal disease with topical nitroglycerin." <i>Dis. Col. Rect.</i> , 38(5):453-456		
	51	Guillermot et al., "Nitroglycerin In Situ Reduces Upper Anal Canal Pressure." <i>Digest. Dis. Sci.</i> , 37(1):155 (1992)		
	52	Guillermot et al., "Action of <i>in situ</i> nitroglycerin on upper anal canal pressure of patients with terminal constipation. A pilot study." <i>Dis. Col. Rect.</i> , 36(4):372-376 (1993)		

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NON PATENT LITERATURE DOCUMENTS					
Examiner Initials *	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.			T ²
(S)	53	Huff et al., (Eds.), "Physicians' Desk Reference." 41st Edition, Medical Economics Company, Oradell, N.J., at pp. 780, 1176-1178, 1533 and 1984-85 (1987)			
	54	Ignarro et al., "Nitric oxide and cyclic GMP formation upon electrical field stimulation cause relaxation of corpus cavernosum smooth muscle." <i>Biochem. Biophys. Res. Commun.</i> , 170:843-850, 1990.			
	55	Jalan, K. et al., "Perineal Wound Healing in Ulcerative Colitis." <i>British Journal of Surgery</i> (October 1969) 56(10):749-53			
	56	Jensen, S. "Treatment of first episodes of acute anal fissure: Prospective randomized study of lignocaine ointment versus hydrocortisone ointment or warm sitz bath plus bran." <i>Br. Med. J.</i> , 292(6529):1167-9 (1986)			
	57	Keighley, R. and Williams, N. "Anatomy and Physiology." Chapter One, in <u>Surgery of the Anus, Rectum and Colon</u> , London, W.B. Saunders (1993)			
	58	Kennedy, M. et al, "Chemical Sphincterotomy for Anal Fissure - A New Treatment." Abstract CR33, presentation at Royal Australasian College of Surgeons at Hobart, Tasmania meeting of May 1-6, 1994			
	59	Kennedy, M. et al., "Glyceryl Trinitrate Ointment for the Treatment of Chronic Anal Fissure." <i>Dis Colon Rectum</i> 42(8):1000-1006 (August 1999)			
	60	Loder, P. et al, "Reversible chemical sphincterotomy" by local application of glyceryl trinitrate." <i>Br. J. Surg.</i> , 81: 1386-1389 (1994).			
	61	Loder, P. et al, "Topical Application of a Nitric Oxide Donor Reduces Internal Anal Sphincter Tone: Therapeutic Implications." <i>Gut</i> 34:S25 (1993) Abstract also published in <i>AGA Abstracts, Gastroenterology</i> , 104: A544 (1993)			
	62	Loder, P. et al., "Topical Glyceryl Trinitrate (GTN): Reversible Chemical Sphincterotomy." Meeting Abstracts, <i>Dis. Col. Rect.</i> , 33:22 (April 1993)			
	63	Lord, P., "A Day-Case Procedure for the Cure of Third-Degree Haemorrhoids." <i>Br. J. Surg.</i> 56(10):47-9 (1969)			
	64	Lubowski, D. et al., "Neural control of internal anal sphincter function." <i>Br. J. Surg.</i> 74: 668-670 (August 1987)			
	65	Lund, J. and Scholefield, J., "A randomised, prospective, double-blind, placebo-controlled trial of glyceryl trinitrate ointment in treatment of anal fissure." <i>Lancet</i> , 349: 11-14 (January 4, 1997)			
	66	Lund, J. et al., "Use of glyceryl trinitrate ointment in the treatment of anal fissure." <i>British Journal of Surgery</i> 83: 776-777 (1996)			
	67	MacDonald, A. et al., "Manual dilation of the anus." <i>British Journal of Surgery</i> 79:1381-1382 (December 1992)			
(S)	68	<i>Mims Annual Drug Reference</i> , Fifteenth Edition, 2-75, page 2042 (1991)			

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	69	O'Kelley, T. et al, "Nerve mediated relaxation of the human internal anal sphincter: the role of nitric oxide." <i>Gut</i> , 34: 689-693 (1993)			
	70	Rattan, S. and Chakder, S., "Role of nitric oxide as a mediator of internal anal sphincter relaxation." <i>Am. J. Physiol.</i> G107-G112 (1992)			
	71	Rattan, S. et al., "Nitric Oxide Pathway in Rectoanal Inhibitory Reflex of Opossum Internal Anal Sphincter." <i>Gastroenterology</i> , 103: 43-50 (1992)			
	72	Shafik, "Role of warm-water bath in anorectal conditions: the thermospheric reflex." <i>J. Clin. Gastroenterol.</i> , 16:304-8 (1993)			
	73	Schouten, W.R. et.al. "Pathophysiological aspects and clinical outcome of intra-anal application of isosorbide dinitrate in patients with chronic anal fissure." <i>Gut</i> 39:465-9 (1996); see also: <i>Dis. Col. Rect.</i> , Apr. 1986, p. 18			
	74	Speakman, C. et al., "Sphincter injury after anal dilation demonstrated by anal endosonography." <i>Br. J. Surg.</i> , 78: 1429-1430 (December 1991)			
	75	Tottrup, A. et al., "Involvement of the L'Arginine-Nitric Oxide Pathway in Internal Anal Sphincter Relaxation." <i>Gastroenterology</i> , 102: 409-41 (1992)			
	76	Watson, S.J. et.al. "Topical glyceryl trinitrate in the treatment of chronic anal fissure." <i>Br. J. Surg.</i> , 83:771-775 (1996)			
	77	Abcarian, "The Role of internal spinchter in chronic anal fissures." <i>Dis. Col. Rect.</i> , 25(6) 525-8 (1982)			
	78	Bacher, H. et.al. "Local nitroglycerin for treatment of anal fissures: an alternative to lateral sphincterotomy?" <i>Dis. Col. Rect.</i> , 40:840-5 (1997)			
	79	Carapeti, E.A. et.al. "Randomised controlled trial shows that glyceryl trinitrate heals anal fissures, higher doses are not more effective, and there is a high recurrence rate." <i>Gut</i> , 44:727-30 (1999)			
	80	Corby, "Anal canal pressures are low in women with postpartum anal fissure." <i>Br. J. Surg.</i> , 84:86-8 (1997)			
	81	<i>Dictionnaire Vidal</i> , Ed. 1996, entries concerning Lenitral Percutane and Lenitral Spray (1996)			
	82	Dodi, "Hot or cold in anal pain? A study of the changes in internal anal spinchter pressure profiles." <i>Dis. Col. Rect.</i> , 29(4):248-51 (1986)			
	83	Farid, M. "Internal anal sphincter relaxation with topical nitroglycerin in the treatment of some benign anal conditions." <i>Br. J. Surg.</i> , 84:1 (1997)			
	84	Farouk, R. et.al. "Changing patterns of treatment for chronic anal fissure." <i>Annual Review College Surgeons England</i> , 80:194-6 (1998)			

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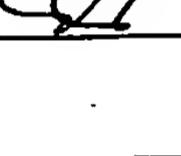
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<i>CR</i>	85	"Glyceryl trinitrate for anal fissure?" <i>Drug and Therapeutics Bulletin</i> ; 36:55-6 (1998)			
	86	Gorfine, S.R. "Topical nitroglycerin ointment for anal fissures and ulcers." <i>New England Journal of Medicine</i> ; 333: 1156-7 (1995)			
	87	Hattori, K. et.al. "Fissure treatment in day surgery days." Presented at the 1998 General Assembly of The Japan Society of Coloproctology (1998)			
	88	Hyman, N.H. et.al. "Nitroglycerin ointment for anal fissures: Effective treatment or just a headache?" <i>Dis. Col. Rect.</i> , 42:383-5 (1999)			
	89	Keck, "Computer-generated profiles of the anal canal in patients with anal fissure." <i>Dis. Col. Rect.</i> , 38(1):72-9 (1995)			
	90	L'Hopital, "Constipation et hypertonie du sphincter interne de l'anus: Response sphincterienne à l'administration sub-linguale de 0,40 mg de NATISPRAY." <i>Gastroenter. Clin. Biol.</i> , 14:268 (1990)			
	91	Lowenstein, B. et.al. Treatment of proctalgia fugax with topical nitroglycerin: report of a case. <i>Dis. Col. Rect.</i> ; 41:667-8. (1998)			
	92	Lund JN et al. "Follow-up of patients with chronic anal fissure treated with topical glyceryl trinitrate." <i>Lancet</i> , 352:1681 (1998)			
	93	Lysy, J. et.al. "Treatment of chronic anal fissure with isosorbide dinitrate: long-term results and dose determination." <i>Dis. Col. Rect.</i> , 41:1406-10 (1998)			
	94	Manookian, C.M. et.al. Topical nitroglycerin in the management of anal fissure: an explosive outcome! <i>American Surgeon</i> 64:962-4 (1998)			
	95	Maria, "Identification of anti-endothelial cell antibodies in patients with chronic anal fissure." <i>Surgery</i> , 126:535-40 (1999)			
	96	Mazier, "Hemorrhoids, fissures, and pruritus ani." <i>Anorectal Surg.</i> , 74(6):1277-92 (1994)			
	97	Oettie, G.J. et.al. "Glyceryl trinitrate vs. sphincterotomy for treatment of chronic fissure-in-ano: a randomized, controlled trial." <i>Dis. Col. Rect.</i> , 40:1318-20 (1997)			
	98	Pitt, J. et.al. "Chemical sphincterotomy for anal fissure." <i>Colorectal disease</i> 1998; 2-8.			
	99	Pitt, "Double-blind, randomized, placebo-controlled trial of oral indoramin to treat chronic anal fissure." ASCRS Meeting, June 2000, Poster Presentation P2 (2000)			
<i>CR</i>	100	Romano, "A critical appraisal of pathogenesis and morbidity of surgical treatment of chronic anal fissure." <i>J. Am. Coll. Surg.</i> , 178:600-4 (1994)			

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	101	Schouten, "Relationship between anal pressure and anodermal blood flow: The vascular pathogenesis of anal fissures." <i>Dis. Col. Rect.</i> , 37(7):664-9 (1994)	
	102	Schouten, "Ischaemic nature of anal fissure." <i>Br. J. Surg.</i> , 83:63-5 (1996)	
	103	Simons, A.J. et al. "Glyceryl trinitrate for anal fissure." <i>Lancet</i> , 348:491-2 (1996)	
	104	Suda, K. et.al. "Application of nitroglycerin ointment on post-hemorrhoidectomy pain." Presented at the 1998 General Assembly of The Japan Society of Coloproctology (1998)	

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